

Appl. No. 09/485 3  
Amdt. dated August 8, 2003  
Reply to Office action of April 9, 2003

**REMARKS/ARGUMENTS**

Claims 8-9, 12-16, and 19-26 currently appear in this application. The Office Action of April 9, 2003, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

**Rejections under 35 U.S.C. 112**

Claims 15-18 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite, the Examiner alleging that the term "kit" renders the claim indefinite.

This rejection is respectfully traversed. Claim 15 has been amended to recite that the kit comprises an effective amount of a selective iNOS inhibitor as a bone mass maintenance drug to maintain bone mass in a pharmaceutically acceptable carrier, and instructions for treating a bone resorption-associated disease. It is clear that claim 15 recites an effective amount of an iNOS inhibitor to maintain bone mass, the inhibitor being in a pharmaceutically acceptable carrier, which is packaged along with instructions as to treat a bone-resorption-associated disease.

Appl. No. 09/485 3  
Amdt. dated August 8, 2003  
Reply to Office action of April 9, 2003

One having ordinary skill in the art could readily appreciate that a kit for treating a bone-resorption-associated disease would include a composition for treating the disease along with instructions for use of the composition. "Instruction" is explaining to the user the method of administration of the active ingredient.

The specification as filed at page 10, lines 4-26, described carriers that can be used with iNOS inhibitors of the present invention, as well as dosage forms and methods for administration. Since the carriers and dosage forms are conventional to one skilled in the art, one skilled in the art having the instructions for administration would be able to administer the iNOS inhibitor properly with minimal experimentation.

#### **Art Rejections**

Claims 8-11 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over The Pharmaceutcial Basis of Therapeutics 19916, hereinafter "Therapeutics", in view of Hukkanen et al. and Moore et al. Therapeutics is said to teach the method of treating osteoporosis by administering estrogen, thereby inhibiting the activity of IL-6. The Examiner concedes that Therapeutics fails to teach a kit comprising L-N-6-(1-iminoethyl)lysine, nor does it teach a method of using the same to treat osteoporosis. Hukkanen et al. are said

Appl. No. 09/485 3  
Amdt. dated August 8, 2003  
Reply to Office action of April 9, 2003

to teach that iNOS inhibitors completely inhibit the activity of cytokines such as IL-6. Moore et al. are said to teach that L-N-6-(1-iminoethyl)lysine is a potent and selective iNOS inhibitor.

This rejection is respectfully traversed.

Therapeutics only teaches that osteoblastic production of IL-6 is reduced by  $17\beta$ -estradiol. Hukkanen et al. only describe the relationship of NOS inhibitors and IL- $1\beta$ . There is nothing at all in Hukkanen et al. merely discuss the production of nitric oxide in regulation of osteoblast and osteoclast metabolism, and there is no teaching or suggesting that iNOS inhibitors affect bone resorption.

As the Examiner is well aware, in order to combine references to render a claimed invention obvious, there must be some motivation to combine the references so as to arrive at the claimed invention. In the present case, Therapeutics discloses that osteoblastic production of IL-6 is reduced by  $17\beta$ -estradiol. Hukkanen et al. describe the relationship of NOS inhibitors and IL- $1\beta$ , but Hukkanen et al. are silent with respect to IL-6, and make no suggestion with respect to NOS inhibitors on bone resorption. The fact that L-N-6-(1-iminoethyl)lysine is a potent and selective iNOS inhibitor is irrelevant, because one skilled in the art reading Therapeutics and

Appl. No. 09/485,333  
Amdt. dated August 8, 2003  
Reply to Office action of April 9, 2003

Hukkanen et al. would not be led to use an inhibitor of IL-1 $\beta$  for inhibiting IL-6.

Furthermore, as is apparent from the documents submitted on January 14, 2003, as evidence of the state of the art, it was shown that NO suppresses bone resorption and that NOS inhibitors promote bone resorption. In view of this evidence, one of ordinary skill in the art would never use iNOS inhibitors for treating osteoporosis.

On the other hand, the present invention was the first to demonstrate that, among NOS inhibitors, selective iNOS inhibitors have a suppressive effect on bone resorption, contrary to the effect of other NOS inhibitors.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.  
Attorneys for Applicant(s)

By 

Anne M. Kornbau  
Registration No. 25,884

Telephone No.: (202) 628-5197  
Facsimile No.: (202) 737-3528  
AMK:nmp

G:\BN\Y\YUAS\END012\Pto\aug 8 03 amend.doc